DETAILED ACTION

1. Claims 42, 44, 45, 47, 48 and 53 were cancelled in the response filed 06/22/2009. All rejections of these claims are now moot. Claims 32-41, 43, 46 and 49-52 are pending.

Claim Rejections - 35 USC § 112 - withdrawn

2. The rejection of claims 32-41, 43, 46 and 49-52 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in view of the amendment filed 06/22/2009.

3. The rejection of claims 32-41, 43, 46 and 49-52 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment filed 06/22/2009.

4. The rejection of claims 39-41 and 52 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment filed 06/22/2009.

Claim Rejections - 35 USC § 102

5. The rejection of claims 32, 35, 43 and 46 under 35 U.S.C. 102(b) as being anticipated by Volpi *et al.* ("Exogenous Amino Acids Stimulate Net Muscle Protein Synthesis in the Elderly," *J. Clin. Invest.*, **1998**, *101*, 2000–2007) is withdrawn in view of the amendment filed 06/22/2009. Volpi *et al.* do not teach oral administration of a composition comprising the amounts of amino acids set forth in claims 32 and 43.

6. The rejection of 43, 46, 49 and 51 under 35 U.S.C. 102(b) as being anticipated by Ozeki *et al.* (US 5,036,052) is withdrawn in view of the amendment filed 06/22/2009. Ozeki *et al.* do not teach oral administration of a composition comprising the amounts of amino acids set forth in claim 43.

7. The rejection of claims 32, 35, 38, 43, 46 and 49 under 35 U.S.C. 102(b) as being anticipated by Dioguardi (U.S. Patent No. 6,218,420) is withdrawn in view of the amendment filed 06/22/2009. Dioguardi does not teach administration of a composition comprising the amounts of amino acids set forth in claims 32 and 43.

8. The rejection of claims 43, 46 and 49 under 35 U.S.C. 102(e) as being anticipated by Conti *et al.* (U.S. 20040192756) is withdrawn in view of the amendment filed 06/22/2009. Conti *et al.* do not teach oral administration of a composition comprising the amounts of amino acids set forth in claim 43.

9. The rejection of claims 43, 46 and 49 are rejected under 35 U.S.C. 102(e) as being anticipated by Conti *et al.* (U.S. 20040157903) is withdrawn in view of the amendment filed 06/22/2009. Conti *et al.* do not teach oral administration of a composition comprising the amounts of amino acids set forth in claim 43.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The rejection of claims 33, 34, 36-41 and 52 under 35 U.S.C. 103(a) as being unpatentable over Volpi *et al.* ("Exogenous Amino Acids Stimulate Net Muscle Protein Synthesis in the Elderly," *J. Clin. Invest.*, **1998**, *101*, 2000–2007), in view of Ozeki *et al.* (US 5,036,052) is withdrawn in view of the amendment filed 06/22/2009. Neither reference teaches oral administration of the composition.

12. Claims 32-41, 43, 46 and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dioguardi (U.S. Patent No. 6,218,420).

Dioguardi teaches a composition comprising, as active ingredients:

up to 75% of the BCAA leucine, isoleucine and valine,

up to 50% of threonine and lysine,

up to 40% of cysteine, histidine, phenylalanine, methionine, tryptophan, tyrosine, characterized in that threonine and lysine are present in larger quantities than the other essential amino acids of the composition, with the exception of the BCAA of the composition (claim 1). The composition is for oral administration (claim 8). The composition is intended for use in a method of preventing and treating inadequate amino acidic introduction and/or overload of less needed amino acids, without interfering with calcium metabolism (col 3, lines 52-67). The ratios of amino acids are consistent with the real needs of a stressed metabolism, with the purposes both of feeding by a sufficient amount of amino acids to cover all amino acids needs and to give the lowest quantity of those necessary amino acids that are utilized in metabolism, thus reducing the load on disposal system of the body by minimizing catabolic products (i.e. urea, uric acid, etc.), without altering calcium excretion (col 3, lines 52-67). Dioguardi teaches that elderly people are in need of this method because even a careful nutrition may not be sufficient to meet body needs (col 2 lines 54-60). Dioguardi teaches that the composition has been tested for safety in chronic use (col 6, line 11).

Dioguardi does not teach the precise relative amounts of amino acids as recited in the instant claims.

MPEP § 2144.05 states: "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" Furthermore, MPEP § 2144.05 states: "A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)" In the instant case, the amount of amino acid in the composition is a result-effective variable because the amino acids are considered active ingredients (see Dioguardi claim 1). Furthermore, Dioguardi teach that the proper ratio of amino acids is critical to achieving the intended goal of the composition and method taught in the prior art.

The limitation in claim 32 regarding maintaining intact, restoring and/or increasing the number of cellular mitochondria and the limitation in claim 43 regarding the treatment of apoptosis of mitochondrial origin, would necessarily be present in the method taught by Dioguardi because the composition, manner of administering it and patient population are present in the prior art.

Response to arguments

In the response filed 06/22/2009, Applicant traverses the rejection on the grounds that Dioguardi does not teach maintaining intact, restoring and/or increasing the number of cellular mitochondria or the treatment of apoptosis of mitochondrial origin. This argument has been

considered but is not persuasive. Dioguardi teach the chronic, oral administration of an amino acid based composition to elderly individuals and motivate the optimization of the amounts and ratios of amino acids in the composition. The method would necessarily result in the effects recited in instant claims 32 and 43 because the composition, manner of administering and patient population are the same as in the prior art.

In the response filed 06/22/2009, Applicant states: "The Examiner's rationale in support of this rejection is completely at odds with the scientific realities relating to methods for treating apoptosis in a subject or for maintaining intact, restoring, and/or increasing the number of cellular mitochondria in an elderly subject. One cannot simply add and subject amino acids or other seemingly therapeutic constituents and expect to have a treatment for a particular condition of a subject. Instead, careful work is required. Such experimentation is anything but routine." This argument represents the opinion of Applicant's attorney, is not supported with evidence and is therefore unpersuasive. MPEP § 2145 states: "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)." In addition, MPEP § 716.01(c) states: "Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, *In re De Blauwe*, 736 F.2d 699,705, 222 USPQ 191, 196 (Fed. Cir. 1984)."

In the response filed 06/22/2009, Applicant traverses the rejection on the grounds that Dioguardi does not teach the claimed ratios and amounts of amino acids. This argument has been fully considered but is not persuasive. As stated above, it would have been obvious to optimize the amounts and ratios of amino acids in the composition taught by Dioguardi. Absent evidence of criticality for the instantly claimed amounts and ratios, the rejection is maintained.

Applicant is reminded of their burden in showing unexpected results. MPEP § 716.02(b) states: "The evidence relied *>upon< should establish "that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992)." MPEP § 716.02(b) states: "[A]ppellants have the burden of explaining the data in any declaration they proffer as evidence of non-obviousness." *Ex parte Ishizaka*, 24 USPQ2d 1621, 1624 (Bd. Pat. App. & Inter. 1992)." MPEP § 716.02(b) states: "Evidence of unexpected properties may be in the form of a direct or indirect comparison of the claimed invention with the closest prior art which is commensurate in scope with the claims. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980)."

Applicants have not met their burden in establishing the criticality of the instantly claimed amounts and ratios of amino acids and have therefore failed to overcome the obviousness rejection over Dioguardi.

13. The rejection of claims 50-53 under 35 U.S.C. 103(a) as being unpatentable over Conti *et al.* (US 20040192756) is withdrawn in view of the amendment filed 06/22/2009. Conti *et al.* do not teach chronic oral administration of the amino acid composition.

14. Claims 43, 46 and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conti *et al.* (U.S. 20040157903).

Conti *et al.* teach a composition comprising the branched chain amino acids leucine, isoleucine and valine, in combination with threonine and lysine and methionine, phenylalanine, histidine and tryphtophan, wherein the sum of the amounts in molecular weights of threonine and lysine is greater than the sum of the amounts of said other essential amino acids being provided, but lower than the sum of the amounts of said branched chain amino acids (claim 4). Conti *et al.* teach a method of administering the composition to improve the myocardial ventricular function in patients suffering from diabetes, a chronic disease (claim 1). Administration is by an oral route (paragraphs 0009, 0045 and 0050). The patient population of instant claim 43 is recited as "a subject" which is generic to the diabetic patients of Conti *et al.* Because diabetes is a chronic disease, administration of the amino acid composition would be chronic.

Conti *et al.* do not teach the precise relative amounts of amino acids as recited in the instant claims.

MPEP § 2144.05 states: "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" Furthermore, MPEP § 2144.05 states: "A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as

routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)" In the instant case, the amount of amino acid in the composition is a result-effective variable because the amino acids are considered active ingredients (see Conti *et al.* claim 4).

The limitation in claim 43 regarding the treatment of apoptosis of mitochondrial origin, would necessarily be present in the method taught by Conti *et al.* because the composition, manner of administering it and patient population are present in the prior art.

Response to arguments

In the response filed 06/22/2009, Applicant traverses the rejection on the grounds that Conti *et al.* do not teach the treatment of apoptosis of mitochondrial origin. This argument has been considered but is not persuasive. Conti *et al.* teach the chronic, oral administration of an amino acid based composition to diabetic individuals and motivate the optimization of the amounts and ratios of amino acids in the composition. The method would necessarily result in the effects recited in instant claim 43 because the composition, manner of administering and patient population are the same as in the prior art.

For this reason, the rejection is maintained.

The applied reference Conti *et al.* (U.S. 20040157903) has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the

effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 43, 46 and 49-52 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6 and 8 of U.S. Patent No. 6,218,420. Although the conflicting claims are not identical, they are not patentably distinct from each other. In the response filed 06/22/2009 Applicant traversed the rejection on the grounds

addressed above with respect to the rejection over Dioguardi. Because Applicant offered no additional arguments, the rejection is maintained.

17. The rejection of claims 43, 46 and 49-52 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 35-39 of copending application 10/486,141 (US 20040192756) is withdrawn in view of the amendment filed 06/22/2009. The '141 Application does not claim chronic oral administration of the amino acids based composition.

18. The rejection of claims 43, 46 and 49-52 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33-54 of copending application 10/332,236 is withdrawn in view of amendments filed in both applications.

19. Claims 43, 46 and 49-52 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-35 of copending application 12/104,722. Although the conflicting claims are not identical, they are not patentably distinct from each other. In the response filed 06/22/2009 Applicant traversed the rejection on the grounds addressed above with respect to the rejection over Conti *et al*. Because Applicant offered no additional arguments, the rejection is maintained. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

20. No claims are allowed.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTINA BRADLEY whose telephone number is (571)272-9044. The examiner can normally be reached on Monday-Thursday, 8:30 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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